EXAMINER'S ANSWER

This is in response to the appeal brief filed 03 September 2002.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because it contains the statement that the "polypeptides of the present invention are useful, for example, for toxicology testing, drug discovery, and disease diagnosis". Whether the claimed polypeptides are useful in the stated capacity is one of the issues to be decided by this appeal.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 1, 2, 12, 21, 42 to 45 and 48 to 51 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 2, 12, 21, 42 to 45 and 48 to 51 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The

instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect.

It is clear from the instant specification that the receptor protein described therein is what is termed an "orphan receptor" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as "NIMPH", or the gene encoding it, the instant invention is incomplete. The

protein encoded by a DNA of the instant invention is a compound believed to function as a receptor simply because its amino acid sequence appears to contain a transmembrane domain. There is no evidence of record that NIMPH is actually expressed at the surface of a cell, binds to a ligand or transduces a signal. The only protein identified in the specification as related to NIMPH also has no demonstrated function. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. The mere fact that this protein is allegedly expressed in cancer cell types, amongst others, is not relevant since thousands of "housekeeping" genes are expressed in all viable nucleated cells. Since the instant specification discloses that NIMPH is not expressed exclusively in cancer cells then there is no evidence to support a conclusion that this protein is diagnostic for a particular cancer. Since the instant specification does not disclose a credible "real world" use for NIMPH then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claims 1, 2, 12, 21, 42 to 45 and 48 to 51 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

6) Claims 2, 21, 42, 44, 45, 48, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. These claims encompass subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 2, for example, encompasses an isolated "naturally occurring" polypeptide having at least 90% sequence identity to the amino acid sequence presented in SEQ ID NO:1 of the instant application. The text in the third paragraph on page 5 of the instant specification indicates that the instant claims are intended to encompass "substantially purified NIMPH obtained from any species, particularly mammalian, including bovine, ovine, porcine, murine, equine, and preferably human, from any source whether natural, synthetic, semi-synthetic, or recombinant ". The instant specification, however, only describes an isolated nucleic acid encoding a single human protein and the disclosure of the "substantially purified polypeptide" encoded thereby is purely prophetic. The only composition which is described in the instant specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed composition was an isolated DNA encoding a single protein having the amino acid sequence presented in SEQ ID NO:1 of the instant application. In the recent decision *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is

claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of an isolated DNA encoding a single human protein having very specific physical and structural properties, the instant specification does not provide a written description of any other isolated nucleic acid or protein and certainly not the very broad genus of protein encompassed by the term "comprising" " a naturally-occurring amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1" or "comprising" "a fragment thereof". As stated in M.P.E.P. 2163 Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement:

"A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. For example, **even though a genetic code table would correlate a known amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native,**

naturally occurring nucleic acid sequence of a naturally occurring mRNA or its corresponding cDNA. Cf. In re Bell, 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993), and In re Deuel, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995) (holding that a process could not render the product of that process obvious under 35 U.S.C. 103). The Federal Circuit has pointed out that under United States law, a description that does not render a claimed invention obvious cannot sufficiently describe the invention for the purposes of the written description requirement of 35 U.S.C. 112. Eli Lilly, 119 F.3d at 1567, 43 USPQ2d at 1405. Compare Fonar Corp. v. General Electric Co., 107 F.3d 1543, 1549, 41 USPQ2d 1801, 1805 (Fed. Cir. 1997)"(emphasis added).

In the same context, whereas an artisan can certainly determine that a specific protein meets the "having at least 90% amino acid identity to SEQ ID NO:1" by reviewing the instant specification, that artisan con not determine if that same protein meets the "naturally occurring" limitation of the instant claims.

(11) Response to Argument

In response to the rejection of claims 1, 2, 12, 21, 42 to 45 and 48 to 51 under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility, Applicant argues that the claimed polypeptides are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established" and "specific". It is noted that toxicology testing and drug discovery are not specifically recited in the specification as originally filed. Each of the alleged uses in toxicology testing, drug discovery, and the diagnosis of disease will be addressed individually, because the facts and issues directed to each use are distinct and separable.

First, Appellant argues that toxicology testing is a well-established utility and concludes that any isolated polynucleotide encoding a naturally occurring polypeptide, including those polypeptides encompassed by the instant claims, could be used in this manner and that the claimed

invention possesses specific and substantial utility in this capacity. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case, as conceded by Appellant, all nucleic acids encoding naturally occurring polypeptides and the polypeptides encoded thereby are in some combination useful in toxicology testing. It is noted that the particulars of toxicology testing with SEQ ID NO:1 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Further, Appellant has failed to identify the consequences of identifying a compound which is toxic to the claimed polypeptide. It is well known that excessive concentrations of common compounds such as sodium chloride and ethanol are toxic to humans. Appellant has not disclosed the practical benefit of determining the toxic (denaturing) concentration of a compound such as sodium chloride or ethanol on a polypeptide of the instant invention. If one does not know the effects that the denaturation of a protein of the instant invention will have on an individual then a knowledge of the minimal concentration of sodium chloride or ethanol which is required to denature that protein is of no immediate practical benefit. Toxicology testing is a general utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but it is not a specific utility with respect to SEQ ID NO:1 because the consequences of denaturing that particular protein are not disclosed, and toxicology testing does not constitute a "well-established" utility.

Appellant urges that the claimed polypeptide can be employed in a disease diagnostic process. Because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. The instant

specification does not identify even a single disease or disorder with which the claimed protein has been credibly associated. Moreover, use of the claimed polypeptide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Appellant's individual polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed "isolated" polypeptide has no "well-established" use. The artisan is required to perform substantial further experimentation on the claimed material itself in order to determine to what "practical use" any expression information regarding this "isolated" polypeptide could be put.

The employment of a protein of the instant invention, or a nucleic acid encoding that protein, in toxicology testing is not a substantial and specific utility. As conceded by Appellant, all human proteins can be employed in such a process irrespective of their normal function. Such utilities are analogous to the assertion that a particular protein can be employed as a molecular weight marker, which is neither a specific or substantial utility. One could just as readily argue that any purified compound having a known structure, such as the steroid compound which was the subject of the *Brenner v. Manson* decision cited above, could be employed as an analytical standard in such processes as nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and mass spectroscopy as well as in polyacrylamide gel electrophoresis (PAGE), high

performance liquid chromatography (HPLC) and gas chromatography. None of these important processes could be practiced without either calibration standards having known molecular structures or, at least, a range of molecular weight markers having known molecular weights. One could further extrapolate upon this premise by asserting that any item having a fixed measurable parameter can be employed to calibrate any machine or process which measures that parameter. For example, any item having a constant mass within an acceptable range can be employed to calibrate a produce scale in a grocery store. The calibration of produce scales is certainly an important function since most states require produce scales to be calibrated and certified. Therefore, to accept Appellant's arguments that any protein of human origin is useful in a toxicology test would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object. It was just such applications that the court appeared to be referring to when it expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the steroid compound which was the subject of that decision had a known structure and molecular weight it could have readily been employed as a molecular standard at that time. Further, because that compound was a hydrocarbon it certainly could have been employed in the well known process of combustion for purposes of lighting and/or the generation of heat. The generation of heat by combustion of hydrocarbons certainly was and remains an important process. Irrespective of such

obvious utilities, the court still held that the compound produced by the process at issue in *Brenner v. Manson* did not have a specific and substantial utility.

To grant Appellant a patent encompassing an isolated naturally occurring human protein of as yet undetermined biological significance based upon Appellant's assertion that any human protein is useful in toxicology testing would be to grant Appellant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" (*Brenner v. Manson, Ibid*). To grant Appellant a patent on the claimed polypeptide based solely upon an assertion that it can be employed in toxicology testing is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a fuel source.

Appellant's arguments that the "REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS" "Misstate the Law" will not be answered by the examiner. The contents of 35 U.S.C., 37 C.F.R., judicial decisions, and guidelines established by the USPTO are not subject to examiner review and will not be questioned or defended by the examiner. These are decisions made by legally empowered government entities to which the examiner is subordinate and those decisions will be followed without question by the examining corps.

The declaration by Lars Furness under 37 CFR 1.132 filed 28 February of 2002 is insufficient to overcome the rejection of claims 1, 2, 12, 21, 42 to 45 and 48 to 51 based upon a

lack of specific and substantial utility as set forth in the last Office action because it merely presents Applicant's arguments of record in declaratory form, such arguments having already been answered on the record.

Appellant's arguments in traversal of the rejection of claims 2, 21, 42, 44, 45, 48, 50 and 51 under 35 U.S.C. 112, first paragraph, as lacking an adequate written description have been answered above in the "Grounds of Rejection". Appellant essentially argues that one of ordinary skill in the art could readily recognized that they were in possession of a protein encompassed by the instant claims by the fact that the protein under consideration meets the limitations recited therein. To the contrary, if one were presented with an isolated protein having an amino acid sequence which is at least 90% identical to SEQ ID NO:1 of the instant application they would not be able to determine if it was encompassed by the instant claims by reviewing the description of the claimed genus which is presented in the instant specification. Of the tens of thousands of material embodiments of proteins encompassed by the limitation "polypeptide having at least 90% amino acid sequence identity to SEQ ID NO:1", only a tiny percentage would also be expected meet to limitation "naturally occurring polypeptide". Because the instant specification does not describe that structural feature or combination of features which distinguishes a polypeptide which meets both of these limitations from a polypeptide which meets only the first limitation, the instant specification does not provide an adequate written description of the claimed genus of polypeptide.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

JOHN ULM
PRIMARY EXAMINER
GROUP 1800

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Conferees

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600